- A method for diagnosing a malignant neoplasm in a
- 2 mammal, comprising contacting a bodily fluid from said
- 3 mammal with an antibody which binds to an human aspartyl
- 4 (asparaginyl) beta-hydroxylase (HAAH) polypeptide under
- 5 conditions sufficient to form an antigen-antibody complex
- 6 and detecting the antigen-antibody complex.
- 1 2. The method of claim 1, wherein said neoplasm is
- 2 derived from endodermal tissue.
- 1 3. The method of claim 1, wherein said neoplasm is
- 2 selected from the group consisting of colon cancer, breast
- 3 cancer, pancreatic cancer, liver cancer, and cancer of the
- 4 bile ducts.
  - 4. The method of claim 1, wherein said neoplasm is
  - 2 a cancer of the central nervous system (CNS).
  - 1 5. The method of claim 1, wherein said bodily fluid
- 2 is selected from the group consisting of a CNS-derived
- 3 bodily fluid, blood, serum, urine, saliva, sputum, lung
- 4 effusion, and ascites fluid.
- 1 6. The method of claim 1, wherein said antibody is a
- 2 monoclonal antibody.
- 1 7. The method of claim 6, wherein said monoclonal
- 2 antibody is FB50.
- 1 8. The method of claim 6, wherein said monoclonal
- 2 antibody is selected from the group consisting of 5C7, 5E9,
- 3 19B, 48A, 74A, 78A, 86A.

- 9. A method for prognosis of a malignant neoplasm of a mammal, comprising
- 3 (a) contacting a bodily fluid from said mammal
- 4 with an antibody which binds to an HAAH polypeptide under
- 5 conditions sufficient to form an antigen-antibody complex
- 6 and detecting the antigen-antibody complex;
- 7 (b) quantitating the amount of complex to
- 8 determine the level of HAAH in said fluid; and
- 9 (c) comparing the level of HAAH in said fluid
- 10 with a normal control level of HAAH, wherein increasing
- 11 levels of HAAH over time indicates an adverse prognosis.
- 1 10. A method of inhibiting tumor growth in a mammal 2 comprising administering to said mammal a compound which 3 inhibits expression of HAAH.
- 1 11. The method of claim 10, wherein said compound is 2 a HAAH antisense nucleic acid.
- 1 12. The method of claim 10, wherein said compound 2 is a ribozyme.
- 1 13. The method of claim 10, wherein said tumor is derived from endodermal tissue.
- 1 14. The method of claim 10, wherein said tumor is
- 2 selected from the group consisting of colon cancer, breast
- 3 cancer, pancreatic cancer, liver cancer, and cancer of the
- 4 bile ducts.
- 1 15. The method of claim 10, wherein said tumor is a
- 2 CNS tumor.

- 1 16. A method of inhibiting tumor growth in a mammal
- 2 comprising administering to said mammal a compound which
- 3 inhibits an enzymatic activity of HAAH.
- 1 17. The method of claim 16, wherein said enzymatic
- 2 activity is hydroxylase activity.
- 1 18. The method of claim 16, wherein said compound
- 2 is a dominant negative mutant of HAAH.
- 1 19. The method of claim 18, wherein said dominant
- 2 negative mutant HAAH comprises a mutation in a catalytic
- 3 domain of HAAH.
- 1 20. The method of claim 16, wherein said compound
- 2 is an HAAH-specific intrabody.
- 1 21. The method of claim 16, wherein said compound
- 2 is L-mimosine.
- 1 22. The method of claim 16, wherein said compound
- 2 is a hydroxypyridone.
- 1 23. A method of inhibiting tumor growth in a mammal
- 2 comprising administering to said mammal a compound which
- 3 inhibits signal transduction through the IRS signal
- 4 transduction pathway.
- 1 24. The method of claim 23, wherein said compound
- 2 inhibits IRS phosphorylation.
- 1 25. The method of claim 23, wherein said compound
- 2 inhibits binding of Fos or Jun to an HAAH promoter sequence.

- 1 26. A method of inhibiting tumor growth in a mammal
- 2 comprising administering to said mammal a compound which
- 3 inhibits HAAH hydroxylation of a NOTCH polypeptide.
- 1 27. The method of claim 26, wherein said compound
- 2 inhibits hydroxylation of an EGF-like repeat sequence in a
- 3 NOTCH polypeptide.
- 1 28. A method of killing a tumor cell comprising
- 2 contacting said tumor cell with cytotoxic agent linked to an
- 3 HAAH-specific antibody.
- 1 29. A monoclonal antibody that binds to an epitope
- 2 of HAAH.
- 1 30. The antibody of claim 29, wherein said epitope
- 2 is within a catalytic site of HAAH.
- 1 31. The antibody of claim 29, wherein said
  - monoclonal antibody is selected from the group consisting of
- 3 5C7, 5E9, 19B, 48A, 74A, 78A, 86A.
- 1 32. The antibody of claim 29, wherein said
- 2 monoclonal antibody is selected from the group consisting of
- 3 HA238A, HA221, HA239, HA241, HA329, or HA355.
- 1 33. A composition comprising a monoclonal antibody
- 2 that binds to an epitope of HAAH linked to a cytotoxic
- 3 agent, wherein said composition preferentially kills tumor
- 4 cells compared to non-tumor cells.
- 1 34. A kit for diagnosis of a tumor in a mammal,
- 2 comprising the antibody of claim 29.

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- The kit of claim 34, wherein said antibody is 1 2 immobilized on a solid phase.
- The kit of claim 35, wherein said solid phase 1
- is selected from a group consisting of an assay plate, an 2
- assay well, a nitrocellulose membrane, a bead, a dipstick, 3
- and a component of an elution column. 4
- A method of determining whether a candidate 1 compound inhibits HAAH enzymatic activity, comprising 2
  - (a) providing a HAAH polypeptide;
  - (b) providing a polypeptide comprising an EGF-like domain;
  - (c) contacting said HAAH polypeptide or said NOTCH polypeptide with said candidate compound;
  - (d) determining hydroxylation of said polypeptide of step (b), wherein a decrease in hydroxylation in the presence of said candidate compound compared to that in the absence of said compound indicates that said compound inhibits HAAH enzymatic activity.
  - 38. A method of determining whether a candidate compound inhibits HAAH activation of NOTCH, comprising
    - (a) providing a cell expressing HAAH;
- (b) contacting said cell with a candidate compound; 4 and 5
- (c) measuring translocation of activated NOTCH to the nucleus of said cell, wherein a decrease in translocation in the presence of said compound compared to 8 that in the absence of said compound indicates that said 9 compound HAAH activation of NOTCH. 10